

Research News

JOURNAL OF HUNTINGTON DISEASE FOUNDATION

PAUL BARNHART, EDITOR

SUMMER 2014

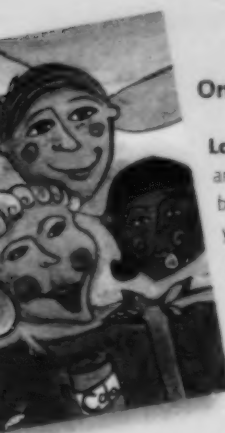
Start

Research shows
that what we eat
affects much more
than our weight

Nutrition

Finish





On the cover

Lorraine Shulba was born and raised in Alberta and began painting at a very young age. She studied fine arts at both Grant MacEwan College and the University of Alberta. Her work has appeared in such publications as *Synchronicity* magazine, *See Magazine*, and *Mosaic* magazine.

AHFMR MISSION

AHFMR supports a community of researchers who generate knowledge, the application of which improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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CONTACT US

Your comments, views and suggestions are welcome. Please forward them to:

The Editor, AHFMR Research News
Alberta Heritage Foundation
for Medical Research
Suite 1500, 10104 - 103 Avenue
Edmonton, Alberta T5J 4A7

Phone: (780) 423-5727

Fax: (780) 429-3509

E-Mail: ahfmrinfo@ahfmr.ab.ca

Internet: www.ahfmr.ab.ca



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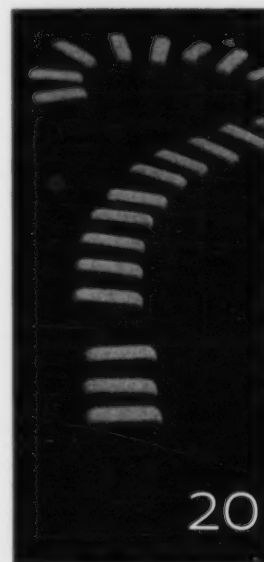
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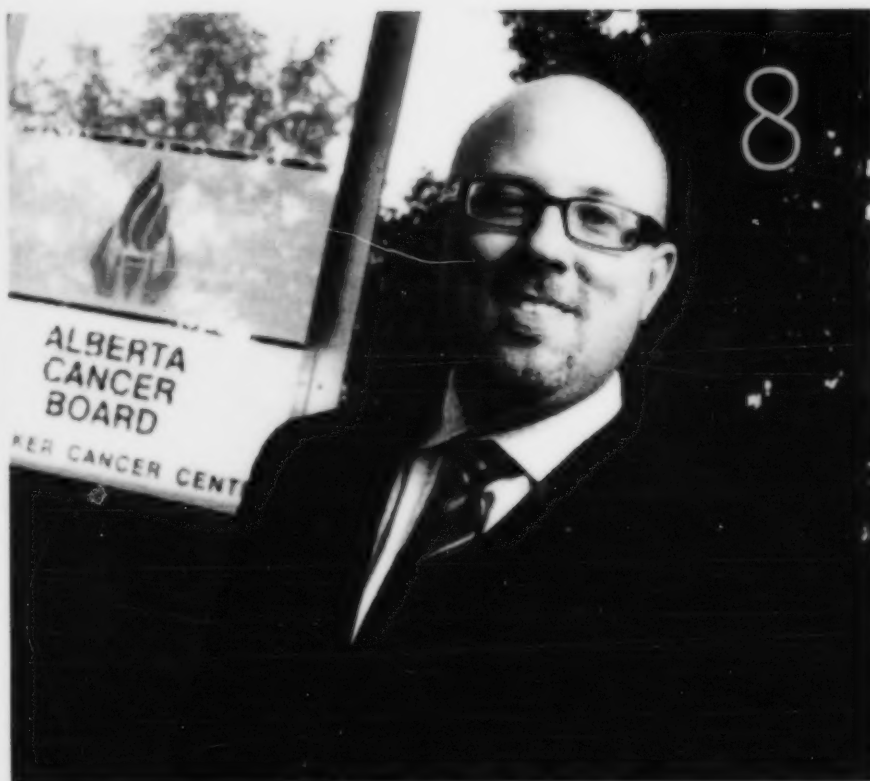


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Production Notes

Executive editor: Kathleen Thurber
 Managing editor: Janet Harvey
 Writers: Connie Bryson, Janet Harvey, Sheelagh Matthews,
 Tara Narwani, Erin O'Connell
 Design: Lime Design Inc.

Cover and feature illustrations: Lorraine Shulba
 Photography and illustration: Trudie Lee, Brian
 Harder, Calgary; Laughing Dog Photography,
 Edmonton; Cindy Revell, Sherwood Park;
 Amanda Woodward, Edmonton; Getty Images

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Accessing medical information

Dr. John Willinsky makes the case for open access to research publications.

WHEN WE LEARN WE HAVE A PARTICULAR HEALTH CONDITION OR DISEASE, MOST OF US SEEK MORE INFORMATION. Increasingly, we search for this knowledge online. Unfortunately, a great deal of information on the Internet is unreliable—anybody with computer access can publish anything they like online, accurate or not. Ironically, in this digital age, the most accurate sources for the latest scientific news and research are often unavailable to the public. Peer-reviewed scientific journals, where scientists publish their research findings, are priced far beyond what many people can afford, and few of these journals are available free of charge online.



DR. JOHN WILLINSKY protests that this should not be the case. "Many complain that the health infor-

mation online is so questionable. I say, of course it is. Only a very small proportion of the *good* medical research has been made freely available online."

The point can be made that the public has a *right* to access this research

The professor of literacy and technology is an outspoken champion of *open access*, which he defines as the publication of research in scholarly journals, available online, without additional fees such as subscription or pay-per-view. According to Dr. Willinsky, open access responds to the public's increasing expectations around access to knowledge. "The public have already shown considerable interest in medical research, and we have to get in line with them," he says. The point can also be made that the public has a *right* to access this research. "The research itself is paid for in good measure by taxpayers or through foundations committed to the public good, so the public's interest in seeing the results from this research makes a kind of ethical and logical sense."

Open access also makes good sense for researchers,

libraries, and policy-makers. It allows researchers' work to be read by more people, including physicians, academics in developing countries, and advocacy groups. Open access assists libraries in making the more than 24,000 existing research journals accessible to researchers and others. (Many of these publications have excessive subscription prices—*Brain Research* tops the list of expensive journals at more than \$21,000 US per year.) It also helps make research available to healthcare policy-makers for use in developing new initiatives. In short, open access helps get research knowledge off the shelf and into the hands of those who can use it to make a difference in people's lives.

Open access also makes good sense for researchers, libraries, and policy-makers

Of course, not everyone thinks that open access is a good thing. The obvious detractors are those who publish research journals, who may see it as a threat to a well-established publishing industry. "In the



academic community, there has long been a particular knowledge economy around publishing that is based on print, on limited circulations, and on the real costs of copy-editing, layout, and distribution," explains Dr. Willinsky. "In the shift to online distribution and online access, we need to find new economic models, as some of these factors have changed."

Many journals and publishers are already adapting. *The New England Journal of Medicine* makes all of its articles available free of charge six months after

they are initially published and made available to subscribers. HighWire Press (a division of the Stanford University Libraries) publishes more than 1,000 journals and has already made 1.6 million articles from these journals available at no cost. PubMed Central and the Public Library of Science also provide free access to many journal articles. Yet there is a long way to go. Dr. Willinsky estimates that only 15% to 20% of the research literature published in journals has also been made available through open access.

Enter the granting agencies. AHFMR and many other research funders are developing policies to make research publications as accessible as possible. In the meantime, Dr. Willinsky suggests that researchers can take up the challenge themselves: many publishers allow the authors of a paper to make the publication available to the institutional repositories at their universities (a sort of digital library). "The public's rising expectations around the right to know is the critical factor," he concludes, "and I think the public has a right to this information."

As you might expect, Dr. Willinsky walks the talk when it comes to this issue. His recently published book on open access is available free of charge online. ☺

Dr. John Willinsky is Pacific Press Professor of Literacy and Technology at the University of British Columbia.

Further reading

Willinsky J. *The access principle: the case for open access to research and scholarship*. Cambridge (MA): MIT Press; 2006.

This book is available free for downloading at the MIT Press online catalogue at <http://mitpress.mit.edu/catalog/item/default.asp?tttype=2&tid=10611>



Celiac disease

Dr. Paul Beck responds to a reader's question about new research and information on celiac disease.



About this feature

AHFMR frequently receives letters requesting information about Heritage research or about various medical conditions. "Responding to the Reader" is a *Research News* feature intended to provide up-to-date information related to readers' questions, with the help of experts in the Alberta research community. AHFMR cannot provide medical advice, however; please see your family physician about your specific health concerns.

CELIAC DISEASE (CD) is caused by an immunological reaction to gluten, a protein found in wheat and grains related to it, including rye, barley, triticale, spelt, and kamut. This immune reaction results in inflammation

or injury (or both) of the small intestine leading to poor absorption of nutrients and, often, diarrhea, abdominal pain, as well as numerous other health problems if it isn't treated.

■ To find out more about new developments in research into celiac disease and its diagnosis and control, we talked with Dr. Paul Beck, an AHFMR Scientist in the University of Calgary's Department of Medicine, and the recipient of several teaching and research awards.

"If you change your diet, you'll get better"

Dr. Beck explains that the treatment for celiac disease is straightforward—patients must eat a gluten-free diet for the rest of their lives. As little as 25 to 50 milligrams of gluten (there are approximately 4,800 milligrams of gluten in one slice of whole wheat bread) can cause inflammation and induce symptoms. Although carefully watching what you eat all the time may be frustrating, the good news is that more

and more gluten-free foods and beverages are showing up on grocery-store shelves. And the Canadian Celiac Association and its local chapters offer tips, resources, and recipes for embarking on a gluten-free lifestyle—and enjoying it.

"While it may be somewhat restrictive, a gluten-free diet isn't all hardship," says Dr. Beck. "What's wrong with a dinner of lobster or steak on a bed of rice with a side of vegetables?" Instead of deprivation, people with celiac disease may find their treatment to be a bit of a gourmet experience. To those who find a gluten-free diet expensive, Dr. Beck points out that celiac patients can get a tax break on their grocery bills to help offset costs.

According to Dr. Beck, though, the foremost benefit of a gluten-free diet lies in significantly lowering the risk of life-threatening diseases associated with the disorder.

Classic symptoms of celiac disease in adults may include diarrhea, nutrient deficiency, non-specific abdominal pain, bloating, flatulence, and fatigue. However, Dr. Beck advises that CD can be a subtle disease, often presenting in nearly undetectable ways that make it hard to diagnose. "When a patient's symptoms are confounding, suspect celiac disease," he recommends.

New blood tests (EMA and tTG) prove very accurate for Marsh 3-level celiac patients—those who show intestinal



inflammation and injury resulting in flattening or blunting of the villi (tiny, finger-like structures that absorb nutrients in the intestine). Yet blood tests for Marsh 1- and 2-level patients (those with less severe intestinal inflammation or injury) often come back with "false negatives", leaving about 30% of patients undiagnosed. However, the gold standard for detecting celiac disease is still a biopsy of the duodenum (the first section of the small intestine). This five- to ten-minute procedure, performed with an endoscope (a long tube with a camera on the end), is relatively straightforward, and has a very low complication rate.

Celiac disease has a strong genetic component

Celiac disease has a strong genetic component: Most common in people of European descent, it is generally rare in those of Asian or African descent, although it appears to be common in some isolated areas in Africa. First-degree (parents, children, siblings) and second-degree (grandparents, grandchildren, nephews, nieces, cousins) relatives of patients with celiac disease are at markedly higher risk, as are those with type 1 diabetes; autoimmune diseases of, for example,

the thyroid or liver; Sjögren's syndrome or other connective-tissue diseases; Down syndrome or Turner's syndrome; and such lesser-known genetic disorders as selective Immunoglobulin A deficiency.

Dr. Beck offers some final food for thought: "CD is a disorder that can be dealt with—if you change your diet, you'll get better." It's that simple. To best succeed at the gluten-free lifestyle, Dr. Beck recommends that patients shift their expectations and understand that it may take anywhere from two weeks to a year to experience the full benefits of a gluten-free diet. ■

About the researcher

Dr. Paul Beck is an *AHFM* Scientist and an associate professor in the Division of Gastroenterology in the Department of Medicine at the University of Calgary.

Selected publication

Devlin SM, Andrews CN, Beck PL. Celiac disease: CME update for family physicians. *Canadian Family Physician* 2004 May;50:719-725.

Recommended websites

Canadian Celiac Association
<http://www.celiac.ca>

Canadian Celiac Association, Calgary Chapter
<http://www.calgaryceliac.com>

Canadian Celiac Association, Edmonton Chapter
<http://www.celiac.edmonton.ab.ca>

Stem-cell research

When it comes to the news about stem cells, it can be hard to distinguish fact from fiction. The media regularly carry stories touting stem cells as cures for everything from baldness to cancer. Is it just hype or real hope?



THE ENORMOUS SCIENTIFIC AND CLINICAL INTEREST IN STEM CELLS IS WELL FOUNDED. These special cells can develop

into many different cell types in the body. When a stem cell divides, each daughter cell can either remain a stem cell or become another type of cell—a blood cell perhaps, or a brain cell or a muscle cell. Because of this versatility, stem cells may be a source of replacement cells for treating diseases and disabilities such as Parkinson's, Alzheimer's, spinal cord injury, stroke, and many more.

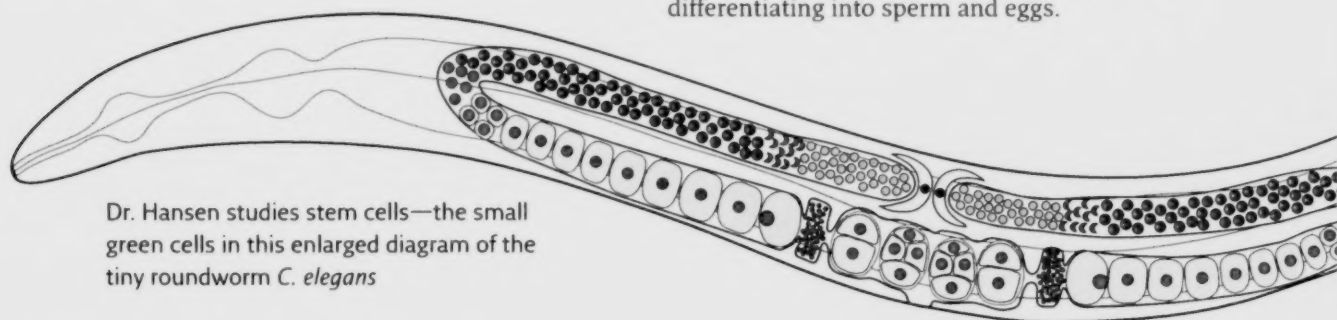
■ THE KEY WORD IS *POTENTIAL*, notes Heritage Scholar Dr. David Hansen. "There's a great deal that we don't understand about stem cells—and this understanding is crucial for realizing the therapeutic potential of stem cells."

Stem cells may be a source of replacement cells for treating diseases and disabilities

In his laboratory at the University of Calgary, Dr. Hansen studies the delicate balance that must be maintained between *proliferation* (the simple self-renewal

of cells) and *differentiation* (where dividing cells turn into different types of cells) in order for stem cells to function properly, and for an organism to develop properly and remain healthy. Too much proliferation can lead to the formation of tumours; too little proliferation will reduce the stem-cell population to the point where it is unable to form an adequate number of specialized cells.

Dr. Hansen is one of many researchers around the world who are attempting to identify the genes involved in regulating this balance. The organism he studies is *C. elegans*, a tiny roundworm—about one millimetre in length—that lives in the soil. He focuses on *germline* stem cells—a very small proportion of germ cells that are capable of either self renewing or differentiating into sperm and eggs.



Dr. Hansen studies stem cells—the small green cells in this enlarged diagram of the tiny roundworm *C. elegans*

Glossary

Stem cells maintain a balance between two basic functions:

- **Differentiation** – when stem cells divide and their daughter cells become specialized cells, such as blood cells
- **Proliferation** – when stem cells divide and their daughter cells remain stem cells, a process called self-renewal.

Germline stem cells – a very small proportion of germ cells that are capable of either differentiation or self-renewal.

Germ cells – reproductive cells, i.e. egg cells or sperm cells.

"It's a case of other cells telling the stem cells what to do"

Although many genes have been identified, how they actually work together to control the balance between stem-cell

proliferation and differentiation is still very much a mystery. "One gene produces proteins that turn on another gene in a kind of cascade that we call a signalling pathway," explains Dr. Hansen. "For the *C. elegans* germ line, one of these pathways—the Notch signalling pathway—is a major regulator of the decision to proliferate or differentiate. But only in one particular location or niche."

Dr. Hansen's team investigates some of the genes involved in maintaining this niche. When stem cells are in this niche, they remain stem

cells. If they leave the niche, they differentiate.

The determining factor is the presence of signalling molecules, which are produced by neighbouring niche cells. "So it's a case of other cells telling the stem cells what to do," says Dr. Hansen. "There is still

It may seem slow to an outsider, but there's real excitement in our lab.

a lot of work to do to figure out how all the components work together.

"The idea behind the research is to try to determine how this

works in relatively simple organisms like worms or fruit flies, and then apply that information to more complex organisms like humans. My work, and that of other scientists, adds incrementally to the knowledge about stem cells. It may seem slow to an outsider, but there's real excitement in our lab. We've been able to gain fundamental insights into how an organism develops and how life is controlled. It's these insights that increase our understanding of stem-cell behaviour in general and will eventually be applicable to human health." =

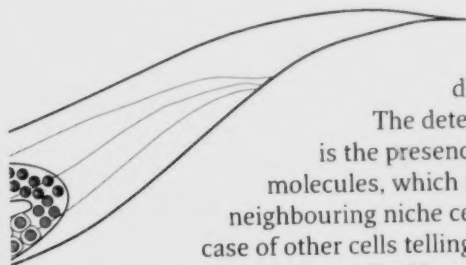


About the researcher

Heritage Scholar Dr. David Hansen is an assistant professor in the Department of Biological Sciences at the University of Calgary.

Selected publication

Hansen D, Schedl T. The regulatory network controlling the proliferation-meiotic entry decision in the *C. elegans* germ line. In: Schatten GP, editor. *Current Topics in Developmental Biology*, vol. 76. Academic Press; 2006. p. 185-215.



Best practices in surgery

If you're about to undergo surgery, you want to know that you will receive the best possible care. Dr. Elijah Dixon is developing a method to define what "best" means.



IS THERE A BETTER WAY TO DO THIS? Even as a medical student, Heritage Population Health Investigator Dr. Elijah Dixon was asking this kind

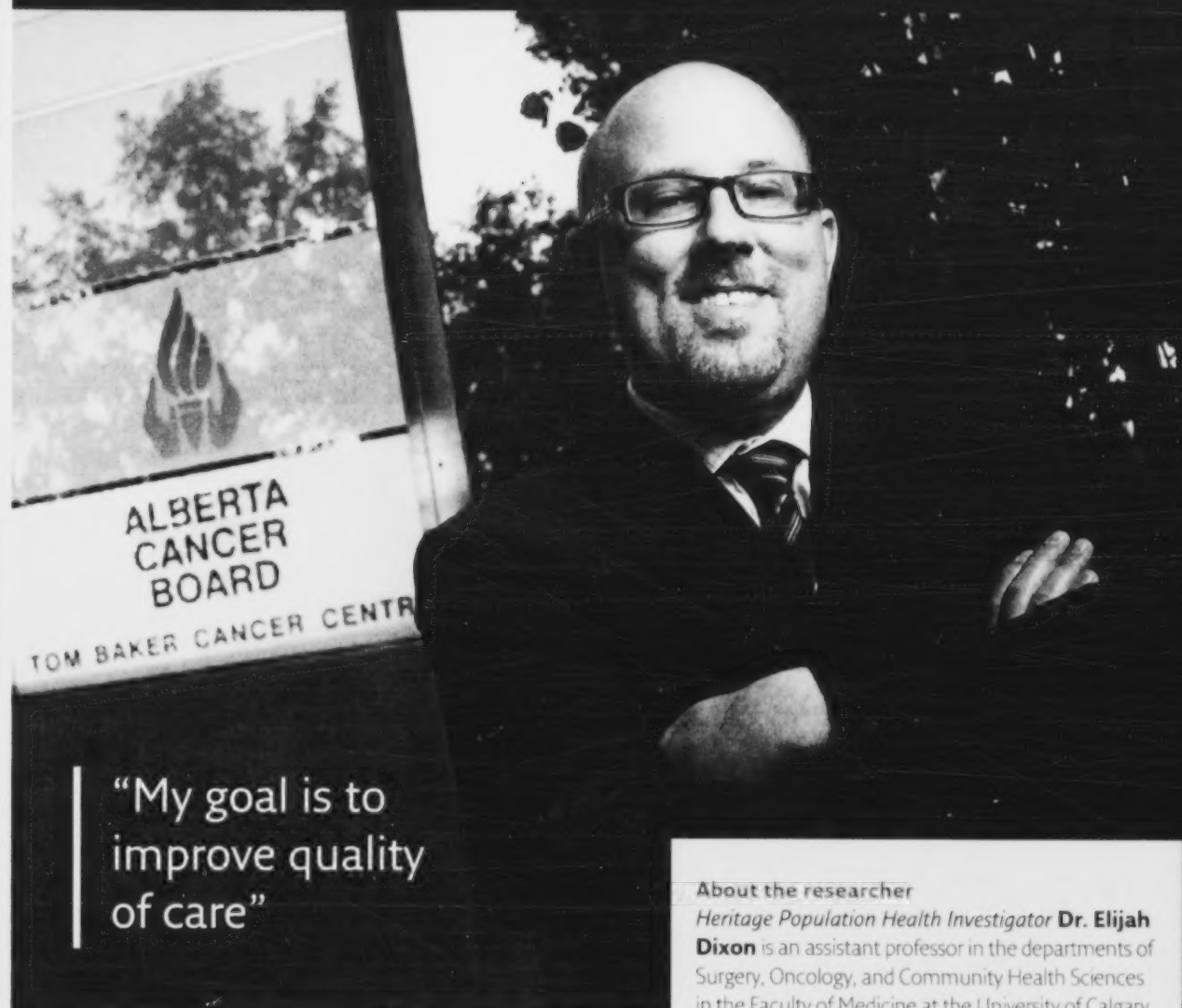
of question. Now it's the focus of his research. The Calgary-based general surgeon, whose clinical specialty is liver and pancreas surgery, has begun a research program to assess surgical procedures.

■ "IT'S EASY TO GET CAUGHT UP in the techniques of surgery and lose sight of the bigger picture: outcomes for patients," he says. "There's a growing recognition that we need to step back and rigorously examine what we do—and not just in surgery, but in all medical specialties."

Dr. Dixon's research goal is to develop a template for the assessment of surgical procedures. As a case study he has chosen a surgery called hepatic resection of metastatic colorectal cancer, which involves removing a portion of the liver. This surgery is an option for many patients whose colorectal cancer (cancer of the colon or rectum) has spread to the liver. Unlike most metastatic cancers, which can spread throughout the body, metastatic colorectal cancer often spreads only to the liver. This means that surgery to remove the cancer from the liver can potentially cure the disease.

The research began in July 2006 and consists of four subprojects:

- **Collecting Canadian data.** The first project assembled and analyzed data on hepatic resection of metastatic colorectal cancer for the past ten years in Canada. The research team now has a picture of the patient population, as well as complications, outcomes, and surgery-related changes over time.
- **Defining quality care.** The second project, currently under way, aims to develop a list of indicators of high-quality care for patients undergoing hepatic resection for metastatic colorectal cancer. It involves a literature review and extensive consultations with a multidisciplinary panel of 16 national experts. (This technique for collecting and distilling knowledge from a group of experts is called a Delphi process.) The team expects to finish this part of the work by the fall of 2007.
- **Validating quality indicators.** Once the list of quality indicators is determined, the third project will commence. It will involve combing through data on patients who have had the surgery in Alberta in the past ten years. The care the patients received will be scored using the quality indicators. Dr. Dixon wants to know whether the scores will correlate with short- and long-term outcomes for these patients.
- **Assessing the impact of surgeon training.** The fourth project will use the Alberta data to investigate whether there is a correlation between patient outcomes and the training of the surgeon who performs the procedure.



“My goal is to improve quality of care”

“My goal is to improve quality of care,” says Dr. Dixon. “To date, we’ve been pretty good at picking out the things that people are not doing well. I’ve always wanted to turn that around and focus on the things that are done well. And that’s what we’re looking at in this research. We’re teasing out the best practices of people, institutions, and systems, and then we’ll make them available so we can all learn what works best.” ❖

About the researcher

Heritage Population Health Investigator Dr. Elijah Dixon is an assistant professor in the departments of Surgery, Oncology, and Community Health Sciences in the Faculty of Medicine at the University of Calgary.

Selected publication

Dixon E, Schneeweiss S, Pasieka JL, Bathe OF, Sutherland F, Doig C. Mortality following liver resection in US medicare patients: does the presence of a liver transplant program affect outcome? *Journal of Surgical Oncology* 2007 Mar 1;95(3):194-200.

Recommended websites

Health Technology Assessment International
<http://www.htai.org>

Canadian Agency for Drugs and Technologies in Health (CADTH)
<http://www.cadth.ca/>



Start

Nutrition

Whether we
eat to live or
live to eat,
nutrition plays
an important
role in our
lives

Finish

Research shows that what we eat affects much more than our weight; nutrition can also influence such things as whether we become ill, the health of our unborn children, and even how we respond to stress.

Society's influence on nutrition

AHFMR HEALTH SENIOR SCHOLAR DR. KIM RAINE, director of the University of Alberta Centre for Health Promotion Studies, wants to explore the changes in our social environment that have led to these behavioural differences. Her aim is to determine the social and ecological causes of obesity. Some have referred to our society as a "toxic environment" in terms of food choices and availability. Dr. Raine suggests that obesity may be a natural response to this toxicity, but she asks, "What are the factors that have created this environment? What is it in our culture that promotes overconsumption and inactivity, as opposed to health?"



■ ONE WAY DR. RAINE HOPES TO IDENTIFY THESE FACTORS is through a program called POWER (Promotion of Optimal Weights through Ecological Research). The POWER team includes AHFMR investigators Dr. Linda McCargar (see story on page 13) and Dr. Noreen Willows and an interdisciplinary team that includes physical activity specialists, a political scientist, an anthropologist, and a geographer, who examine the various factors affecting weight from the perspective of their specialties. The initiative also focuses on such vulnerable populations as low-income neighbourhoods, aboriginal communities, and children. "We want to know if these groups have fewer resources to resist the 'toxic environment,'" explains Dr. Raine (see "Mapping the food landscape" on page 12 for some examples of POWER projects).

Health promotion is an action-oriented field, says Dr. Raine, so she and her co-investigators don't just want to understand the problem,

Research shows that what we eat affects much more than our weight; nutrition can also influence such things as whether we become ill, the health of our unborn children, and even how we respond to stress.

Tell me what you eat and I will tell you what you are. Those words, written by the 19th-century food connoisseur Anthelme Brillat-Savarin, referred to the pleasures of the table. With obesity on the rise around the world, the words have a different resonance in modern society. In 2000 the World Health Organization (WHO) estimated that, worldwide, at least 400 million people were obese. That number is projected to increase to 600 million by 2015, and WHO has referred to obesity as a global health epidemic. Rates of obesity and overweight have increased dramatically over the past 50 to 60 years. Scientists point out that our genetic makeup has not changed sufficiently over this time quarter-century to provide a biological explanation for this shift. But something else has changed in that time frame: our eating habits. People are eating more, eating different types of food, and increasingly, sitting on the couch.



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Health promotion is an action-oriented field, says Dr. Raine, so she and her co-investigators don't just want to understand the problem,

Obesity is now a societal problem, not an individual issue

they also want to help fix it. Their research will lead to recommendations and strategies to promote good nutritional choices and healthy body weight. "The idea is to create a culture where healthy eating, and taking the time to do it, is normal." This may involve such changes as removing soft-drink vending machines from schools, providing health and nutrition education, and making healthy food choices more affordable and accessible.

In our fast-paced, supersized world, these may seem like tiny steps on an uphill road. But Dr. Raine derives hope from the lessons learned in the campaign for tobacco reduction. Today tobacco is recognized as a highly addictive and dangerous substance, advertising is tightly regulated, access to tobacco for minors is restricted, and smoking is prohibited in many public places. Not so long ago these changes would have been incomprehensible, even offensive to some people. Similarly, even two years ago many would have seen the removal of soft-drink machines from schools as too restrictive, but it's starting to happen.

Obesity is now a societal problem, not an individual issue, Dr. Raine emphasizes. "The idea is slowly becoming more accepted that when this many people are obese, it's not just an issue of lack of willpower."

Mapping the food landscape

In 2004, when he was a master's student at the University of Alberta, Eric Hemphill mapped the locations of fast-food restaurants and supermarkets in Edmonton, then compared his map to census information. He found that lower-income neighbourhoods (those with higher percentages of low-income residents, single parents, renters, and immigrants) had 2.7 times more fast-food outlets than higher-income communities. He also discovered that Edmonton had 761 fast-food outlets and only 61 supermarkets.

For her 2006 master's thesis, Leia Minaker, mapped the food environment on the University of Alberta campus, documenting locations of food outlets, advertising, hours of operation, length of lineups for service, and a number of other factors. She found that burger and doughnut shops were the cheapest sources of calories on campus, and cafeterias the most expensive. A dozen doughnuts was the cheapest food available at \$0.18 per 100 calories. A salad cost \$9.78 for 100 calories.



About the researcher

Dr. Kim Raine, an *AHFMR Health Senior Scholar*, is a full professor at the School of Public Health and director of the Centre for Health Promotion Studies at the University of Alberta. She is also a registered dietitian.

Selected publication

Raine KD. Determinants of healthy eating in Canada: an overview and

synthesis. *Canadian Journal of Public Health* 2005 Jul/Aug;96(Suppl 3):S8-S14.

Recommended website
POWER (Promotion of Optimal Weights through Ecological Research)

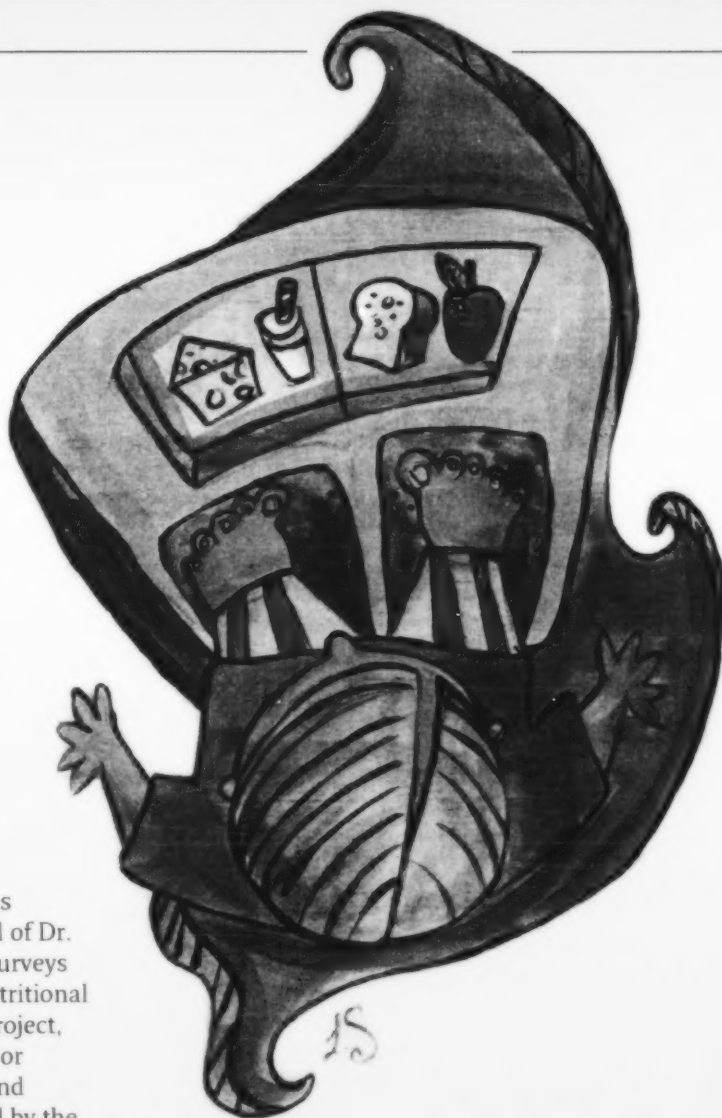
<http://www.power.ualberta.ca>

Nutrition and body weight

ONE OF DR. RAINE'S COLLABORATORS at the University of Alberta, Dr. Linda McCargar, looks at body weight on an individual rather than a societal level. She examines the physiological factors that influence body weight, and her specific interests include metabolic rate and body composition. Metabolic rate is the rate at which the body uses energy; body composition is the percentages of bone, lean and fat tissue in the body as influenced by three major things: diet, physical activity, and disease.

■ **THESE THREE FACTORS AND THE ROLES THEY PLAY IN BODY WEIGHT** are key to all of Dr. McCargar's research. In one project she surveys Alberta teens about their body weight, nutritional habits, and physical activity. In another project, she works with patients who have cancer or diabetes to determine the effects of diet and physical activity, as well as the role played by the disease.

One of Dr. McCargar's new areas of interest is *sarcopenic obesity*, which occurs in people with low muscle mass who also have a high percentage of body fat (most commonly observed in older people). Improved equipment for accurately measuring body composition has led to a clear description of this new subgroup. "Studies suggest that low muscle mass is detrimental to health and functional status; and these individuals can have difficulty with activities of daily living," explains Dr. McCargar. "We already know that high body fat is associated with health risks; so when the two are combined, it is an even greater concern."



Throughout her career Dr. McCargar's overriding interest has been finding strategies for successful weight loss. "We know that certain dietary treatments work well in the short term, but how to sustain weight loss is still not well established." She explains that the little information available suggests that continued vigilance regarding diet and physical activity is the answer—a message that can be difficult to hear for people who have struggled for many years to lose weight. "We want to know if there are alternate ways to maintain a healthy weight, perhaps by adding more variety to your physical activity patterns or to your dietary patterns?"

"When it comes to nutrition, we know so much more than we did ten years ago"

Looking at both weight loss and weight gain gives Dr. McCargar a broader picture of the factors at work. "It is often thought that metabolic rate is reduced in situations of overweight and increased in situations of underweight, but that doesn't necessarily seem to be the case," she explains, adding that many variables seem to be at play.

"When it comes to nutrition, we know so much more than we did ten years ago," says Dr. McCargar. "And with public interest so high, it's a very exciting time to be working in this field."



About the researcher

Dr. Linda McCargar is a registered dietitian and a full professor in the Department of Agricultural, Food and Nutritional Science at the University of Alberta. She receives support through the **Health Research Fund**, administered by AHFMR on behalf of Alberta Health and Wellness.

Selected publication

Barbarich BN, Kubrak C, Hanning R, McCargar L. 19. Combined diet and exercise in the treatment of pediatric overweight and obesity. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children (Obesity Canada Clinical Practice Guidelines Expert Panel). *Canadian Medical Association Journal*. 2007 April 10;176(8 Suppl 1): Online 87-88. Available from: <http://www.cmaj.ca/cgi/content/full/176/8/S1/DC1>



The Human Nutrition Research Unit

Dr. McCargar is the director of the Human Nutrition Research Unit at the University of Alberta. This is a research facility that has it all. Established in 2002 to support nutrition research in western Canada, it is home to the latest equipment for measuring body composition and metabolism. The unit is also equipped to analyze nutrition and physical activity with everything from hand-grip tests and walking assessments to lifestyle questionnaires and focus groups.

For more information check out the website at <http://www.hnru.afns.ualberta.ca/>

Alberta Institute for Human Nutrition

The Alberta Institute for Human Nutrition is a designated research institute at the University of Alberta. Under the direction of Dr. Tom Clandinin the institute brings together nutrition researchers at the university and from other parts of the province in such diverse fields as medicine, pediatrics, pharmacology, and physical education.

Nutrition, exercise, and type 2 diabetes

DOWN THE HALL FROM DR. McCARGAR'S OFFICE you can find Dr. David Wright, whose research focuses on the effects of diet and exercise on metabolism in fat and muscle tissue. After completing graduate work in exercise physiology and metabolism in the United States, Dr. Wright hoped to find a faculty position in western Canada. An AHFMR Scholar award brought him to the University of Alberta in July 2006.

■ **TYPE 2 DIABETES AND OBESITY** are the big picture for Dr. Wright. He points out that we have known for 30 or 40 years that exercise can improve insulin sensitivity and prevent the development of type 2 diabetes. "However, the sad reality is that people aren't exercising, we're getting fatter as a country, and the incidence of type 2 diabetes is increasing."

So Dr. Wright wants to figure out just *how* exercise improves insulin sensitivity. He hopes to determine the beneficial effects of exercise as it relates to insulin, and identify the mechanisms involved, in order to mimic those effects through nutrition. "People with type 2 diabetes probably can't exercise at a high enough intensity or for a long enough duration to induce some of the benefits of exercise," he explains. "So if we can find non-pharmaceutical interventions which have the same effects, it could have a very big impact on healthcare delivery."

To study these questions, Dr. Wright induces insulin resistance in rodents by feeding them

high-fat diets for 6 to 8 weeks. Once he identifies the actual changes leading to insulin resistance, he will try to prevent them with exercise or with certain nutritional treatments.

Dr. Wright thinks that fat tissue may be one of the key culprits in the development of insulin resistance. He explains that for years fat was considered nothing more than inert, unsightly tissue. However, research has suggested that fat is an active endocrine organ, secreting many factors capable of influencing insulin action in the body. "I'm hypothesizing that one of the initial defects in the development of whole-body insulin resistance occurs in fat tissue," he explains.

The Alberta Diabetes Institute

Like many nutrition researchers at the University of Alberta, Dr. Wright will relocate to the Health Research Innovation Facility once it is completed. This building (AHFMR contributed \$20 million towards its construction) will house the Alberta Diabetes Institute, where researchers will study diabetes from a variety of angles—from basic research to more applied work and everything in between. "It will be a very good environment for my work," says Dr. Wright.



About the researcher
Dr. David Wright is an *AHFMR Scholar* and assistant professor in the Department of Agricultural, Food and Nutritional Science at the University of Alberta.

Selected publication

Wright DC, Han D-H, Garcia-Roves PM, Geiger PC, Jones TE, Holloszy JO. Exercise-induced mitochondrial biogenesis begins before the increase in muscle PGC-1 expression. *Journal of Biological Chemistry* 2007 Jan 5;282(1):194-199.

Dr. Wright wants to figure out just *how* exercise improves insulin sensitivity

Nutrition and disease

UNIVERSITY OF CALGARY NUTRITION

RESEARCHER DR. RAYLENE REIMER studies the role of diet in heart disease, obesity, and type 2 diabetes. One of her interests is the link between obesity and *prebiotic fibre*, a unique dietary fibre that increases the number of healthy bacteria living in the gut. "Research has shown that increasing these bacteria can improve the overall health of your gut and maybe your immune system," says Dr. Reimer. "So we were interested in looking at prebiotic fibre for some of its other properties: perhaps its ability to help people reduce their food intake and ultimately to help them with weight loss." Some initial studies showed that the fibre had good results in rats: Those that received the fibre significantly reduced their food intake, and their body-fat percentage decreased. Dr. Reimer has just completed a three-month study with the fibre in overweight and obese humans, and the initial findings look promising.

■ **ANOTHER BRANCH OF HER STUDIES INVOLVES DAIRY PROTEINS.** Evidence from epidemiological studies has suggested that the more dairy products an individual consumes, the lower their weight and body-fat percentage. Dr. Reimer has examined the effect of a diet high in dairy protein on obese

rats, with some dramatic effects. Rats on skim milk diets gained less weight than those on diets without. Dr. Reimer is currently seeking ethics approval for a human study to follow up on these results. She now wants to identify the mechanism by which skim milk reduces weight gain.

The area of research that Dr. Reimer finds most intriguing is early dietary programming: the idea that maternal diet before a child is born, or the diet an infant receives after birth, can permanently program the child's genes for increased or decreased risk for heart disease, obesity, and type 2 diabetes. To study this phenomenon, Dr. Reimer examines the effects of controlled standard diets, high-fibre diets, and high-protein diets on both pregnant rats and rat pups. Her most interesting finding came when she gave the rats high-fat, high-sugar diets as adults. The rats ex-



Dr. Reimer has examined the effect of a diet high in dairy protein

posed to high-protein diets as pups had the most dramatic increases in body weight and body-fat percentage—the diets they had received when young seemed to alter their metabolisms.

This type of early-programming research is especially hot right now, explains Dr. Reimer. “If we’re ever going to get a handle on slowing down the obesity epidemic, we have to look at prevention as a strategy. And prevention may go even further back than we thought—to the first year of life, to what the mother eats during pregnancy, even to pre-conception.”



About the researcher

Dr. Raylene Reimer is a registered dietitian and an associate professor in the Faculty of Kinesiology and the Faculty of Medicine (Department of Biochemistry and Molecular Biology) at the University of Calgary.

Selected publication

Reimer RA, Russel JC. Glucose tolerance, lipids and GLP-1 secretion in JCR:LA-cp rats fed a high-protein fiber diet. *Obesity*. In press 2007.

Nutrition and the stress response

WE’VE ALL HEARD THAT WE SHOULD AVOID FOODS THAT ARE HIGH IN FAT. But now we may have a new reason for doing so. Research at the University of Calgary has found that a single high-fat meal can elevate your stress response.

■ “WE WERE INTERESTED IN THE EFFECTS of different types of meals on cardiovascular responses to stress,” says Dr. Tavis Campbell, assistant professor in the Department of Psychology at the University of Calgary. “The idea is that exaggerated or prolonged responses to stress are associated with the development of sustained high blood pressure.”

Dr. Campbell set out to examine the effects of high-fat meals on the stress response. Study participants came to the lab on two separate occasions following a night of fasting. One day they ate high-fat breakfasts from McDonald’s. Within a week the same participants ate low-fat breakfasts. (In order to keep the calorie and sodium levels equal, this low-fat meal contained higher sugar and carbohydrate content to replace the fat content.) Dr. Campbell emphasizes that the study did not examine a healthy alternative breakfast, but only studied the effects of the high-fat vs. low-fat meals.

After eating each meal, participants rested for two hours, then performed a series of standardized stressor tests including completing a math test, immersing their hands in icewater, experiencing the uncomfortable pressure of inflated blood pressure cuffs on their arms, and speaking to a group about emotionally provocative events. The investigators recorded several cardiovascular measures including blood pressure, heart rate, and vascular resistance (the resistance that must be overcome to push blood through the circulatory system).

Dr. Campbell set out to examine the effects of high-fat meals on the stress response

After consuming the high-fat meal, participants demonstrated exaggerated stress responses to physical and mental stress. Blood pressure and vascular resistance responses were 1.5 times higher than after the low-fat meal. "These were striking effects after only one meal," notes Dr. Campbell.

Dr. Campbell sees this work as part of other research efforts to combat obesity and the health conditions that go with it, an emerging field for psychologists in Canada. "When we think about what drives chronic illness, the major contributors are behaviour and lifestyle choices," he explains. "Look at the major killers: More than 50% of cancers can be explained by health behaviours such as smoking and diet. Cardiovascular disease is driven primarily by overweight, obesity, and lack of exercise. Psychologists are experts in behaviour change. We can play a role in prevention." *



About the researcher

Dr. Tavis Campbell is a clinical psychologist and assistant professor in the Department of Psychology at the University of Calgary.

Selected publication

Jakulj F, Zernicke K, Bacon SL, van Wieringen LE, Key BL, West SG, Campbell TS. A high-fat meal in-

creases cardiovascular reactivity to psychological stress in healthy young adults. *Journal of Nutrition* 2007 Apr;137(4):935-939.

Recommended website Canadian

Hypertension Society
<http://www.hypertension.ca/>

Backlash

Not everyone was happy with the results of Dr. Campbell's study. A written statement issued by McDonald's Canada spokesman Ron Christianson in response to the research read: "Based on the information that we do have, this work does not appear to be representative of our customers or the menu options and portion sizes we offer, and makes broad conclusions."

The research also touched off a storm with some supporters of low-carbohydrate diets. Dr. Campbell received several angry e-mails from advocates of Atkins and other low-carb diets (which tend to be higher in fat) and his study was the subject of a great deal of debate in the blogosphere. "People on low-carb diets may feel like this study somehow invalidates their efforts, but it really had nothing to do with that," explains Dr. Campbell.

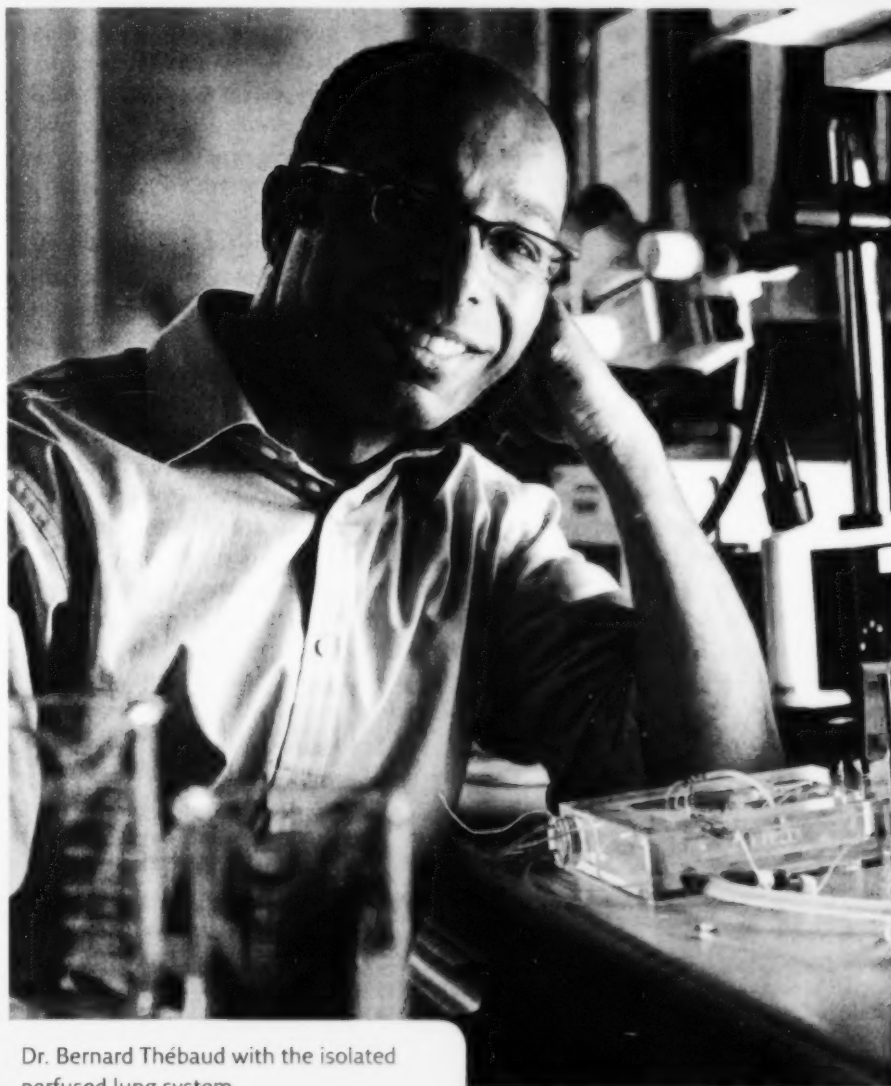
"I think the controversy highlights the serious challenges involved in promoting healthy eating."

Exploring uncharted territory in the body

The first microscope, invented during the 17th century, was little more than a powerful magnifying glass mounted on a brass plate. Obviously science has made considerable progress, but who could have imagined the technology that today's researchers would have at their fingertips? Technology such as the Cellvizio.

The Cellvizio consists of three connected parts: a microprobe, a laser scanning unit, and a computer with specialized software. Its major innovation lies in the microprobe made of tiny tubing that carries the scanning laser microscope into the body. This probe can be inserted into an animal's lung, digestive tract, or anywhere else it fits, allowing scientists visual access to minute structures. The Cellvizio uses fibre optics (thin strands of flexible plastic) to transmit light onto the body tissues, which reflect that light at certain wavelengths corresponding to the density of the tissue. The Cellvizio's laser scanning unit converts the reflected light into an image which researchers can see on their computer screens. With the Cellvizio-LUNG version, for example, the scanning unit recognizes the wavelength of light reflected by lung tissue, allowing researchers to view the actual airsacs (*alveoli*) in microscopic detail.

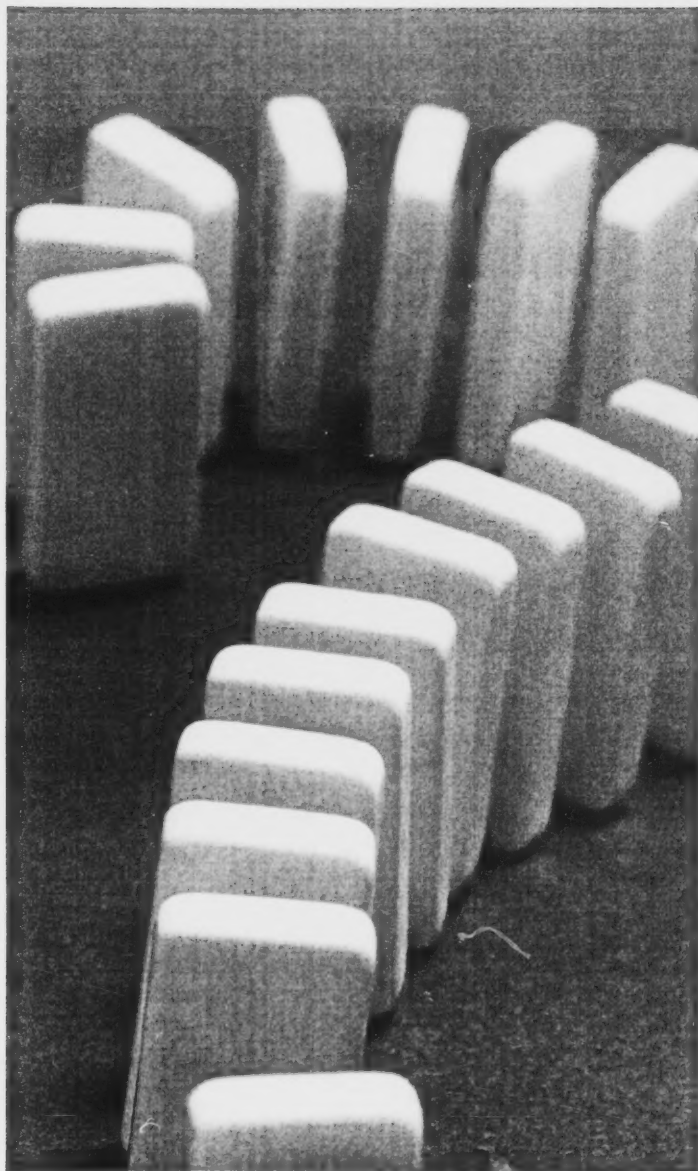
AHFMR Clinical Investigator Dr. Bernard Thébaud combines the Cellvizio with other equipment, such as the Hugo Sachs isolated perfused lung system (which mea-



Dr. Bernard Thébaud with the isolated perfused lung system

sures various lung dynamics), to research lung development, injury, and repair in a mouse model of premature lung development. The Cellvizio could provide key insights that lead to improved treatment for breathing problems in preterm babies. ❖

Heritage Clinical Investigator Dr. Bernard Thébaud received an **AHFMR Major Equipment Grant** to purchase the Cellvizio and the isolated perfused lung system.



"WHEN I GROW UP, MY MIND AND BODY

AS THESE CHILLING WORDS TESTIFY, a diagnosis of Huntington's disease is currently a life sentence. The inherited disease, which primarily affects adults, causes certain parts of the brain to degenerate. It begins with uncontrollable body movements, and complications associated with severe impairment of motor function ultimately lead to death. Such drugs as antidepressants deal with some of the symptoms, but there is no cure for Huntington's disease. On average, patients die within 15 to 20 years of diagnosis.



FRAMED BY A PANORAMIC VIEW OF THE UNIVERSITY OF ALBERTA HOSPITAL from her office in the Department of Pharmacology, Dr. Simonetta Sipione explains the challenges researchers have faced in

developing a treatment for Huntington's disease. When the gene that causes it was discovered in 1993, many hoped that the information would lead to an understanding of the disease within a few years. But almost fifteen years later, researchers still don't know how a mutation in this one gene causes so many severe symptoms. What is clear is that much of normal cell physiology is dysfunctional in the nerve cells of people who have Huntington's disease. For example, the energy-producing centres of the cell (the mitochondria) don't function properly.

Cell signalling (the way a cell converts a stimulus into an appropriate action) is also impaired.

Dr. Sipione often uses an analogy when

explaining what happens in Huntington's cells. "Imagine a complex of dominoes. A ball hits two or three initial dominoes, but then each of these tips over a string of other dominoes. It's a cascade effect. If you imagine that the ball is

Huntington's disease

Fifteen years after the discovery of the gene that causes Huntington's we still don't have a clear understanding of this incredibly complex disease.

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A domino-like cascade effect occurs in Huntington's cells

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Huntington's disease

Fifteen years after the discovery of the gene that causes Huntington's we still don't have a clear understanding of this incredibly complex disease.

WILL SLOWLY DETERIORATE UNTIL I CHOKE TO DEATH TRYING TO SWALLOW."

— HUNTINGTON SOCIETY OF CANADA PUBLIC SERVICE ANNOUNCEMENT

Scientists would like to identify the early changes induced by Huntington's disease

mutant huntingtin (the protein produced by the HD gene) and each domino is a cell function: at a certain point in the cascade it's very difficult for

researchers to determine what's primarily due to mutant huntingtin, and what's just a consequence of general cell dysfunction."

Scientists would like to identify the very early changes induced by Huntington's disease, as these would be the best targets for therapies. Dr. Sipione may have stumbled upon one of these early changes in 2002 while completing her post-doctoral work at the University of Milan. In an experiment designed to identify all the genes that are turned on and off upon activation of the mutant huntingtin protein, she observed that several genes involved in producing cholesterol didn't function normally. Many of the impaired pathways in Huntington's cells could therefore be linked to the reduced availability of cholesterol.

This research is her "pet project", and she now returns to it as a new AHFMR Scholar. She began setting up her lab last September. Pending the arrival of her new graduate students early this summer, Dr. Sipione is still actively involved in running her own experiments, and she dons her white lab coat almost daily. Her first questions are whether low cholesterol levels actually result in altered cell signalling in Huntington's disease, and whether restoring cholesterol to normal levels can restore proper cell signalling.

Despite indications that cholesterol (or the lack of it) may play a central role in the development of Huntington's disease, Dr. Sipione stresses that treatment would not involve simply supplying patients with more cholesterol in their diets. Dietary cholesterol cannot enter the brain. The key to treatment will be a better understanding of how the production of cholesterol in the brain is controlled. Even then, because Huntington's is such a complex disease, Dr. Sipione believes that future treatment will likely involve administering

a combination of drugs, or targeting a set of pathways simultaneously. This reality forces her to be cautious in predicting when patients might expect a cure.

But she is also optimistic, knowing that scientific progress is exponential: one discovery leads many groups to start approaching the question from different angles. Dr. Sipione is certainly ready. *



About the researcher

Dr. Simonetta Sipione is an *AHFMR Scholar* and an assistant professor in the Department of Pharmacology, part of the Faculty of Medicine and Dentistry at the University of Alberta.

Selected publication

Sipione S, Rigamonti D, Valenza M, Zuccato C, Conti L, Pritchard J, Kooperberg C, Olson JM, Cattaneo E. Early transcriptional profiles in huntingtin-inducible striatal cells by microarray analyses. *Human Molecular Genetics* 2002;11(17):1953-1965.

Recommended websites

Huntington Society of Canada

<http://www.hsc-ca.org/>

Huntington's Disease Society of America

<http://www.hdsa.org>

Hereditary Disease Foundation

<http://www.hdfoundation.org>



Biofilm busters

Calgary-based biotech firm Innovotech is developing new ways to screen and treat biofilms, the culprits behind 60% of human bacterial infections, says president Ken Boutilier.

About ForeFront

AHFMR's ForeFront programs work to apply health research into innovative products and services that lead to improved health.

For more information go to <http://www.ahfmr.ab.ca/forefront>

WELCOME TO SLIME CITY—home to most of the world's bacteria. Although we tend to think of bacteria as free-floating single cells, most of them live together in large numbers, attached to a surface and surrounded by the slime they secrete.



THE REAL NAME for these bacterial communities is *biofilms*. They're ev-

erywhere—in the slime on river stones, in the plaque on teeth, in the coatings inside water pipes. According to the US Centers for Disease

Control and Prevention, as many as 60% of human bacterial infections in the Western world are caused by biofilms. These include infections of the urinary tract and the middle ear; infections that develop around catheters and devices such as joint prostheses and heart valves; as well as infections caused by a wide range of conditions, from cystic fibrosis to gum disease.

Biofilms are big problems because they're very hard to kill. Current antibiotics are designed to fight free-floating bacteria, which are relatively easy to kill. When those same bacteria form a biofilm, their resistance to antibiotics can become as much as 4,000 times stronger. Now Innovotech, a small Alberta biotech company, is leading the way in the screening and testing of biofilms—the first important steps in effectively treating the infections associated with them.

Innovotech's technology has its origins in biofilm research led by Dr. Merle Olson and Dr. Howard Ceri at the University of Calgary. Their group invented and patented a specialized testing system for biofilms, and created a company called MBEC BioProducts to market it.

The MBEC Assay is a screening system for growing and experimenting on biofilms. It is designed to determine whether a drug that is effective against free-floating bacteria can eradicate the same organisms in a biofilm.

Biofilms are big problems because they're very hard to kill

MBEC amalgamated with Innovotech in 2006, and the company is going full throttle developing products that address biofilm problems in a range of industries. Innovotech's newest product is the bioFILM PA antimicrobial sensitivity kit, which quickly identifies the combination of antibiotics that will kill biofilms formed by *Pseudomonas aeruginosa* bacteria. No other test can do this. These biofilms often develop in the lungs of cystic fibrosis patients, where they may cause pneumonias which are potentially lethal.

"As bacteria become more resistant to antibiotics, the use of combinations of antibiotics is increasing," says Innovotech president Ken Boutilier. "Our



Innovotech's antimicrobial kit

technology allows clinicians to make better use of currently available drugs by providing a much clearer picture of the effectiveness of antibiotic combinations against a specific patient's biofilm infection. This should result in better patient outcomes and reduced healthcare costs."

The company received Phase 2 funding from AHFMR's ForeFront Innovation Program to advance the development of this product. The ForeFront

"We may be a small company, but we've got big plans."

program funds medical technologies that demonstrate potential to improve health care and achieve commercial success.

And there's another AHFMR connection to Innovotech: one of the Innovotech staff who worked on bioFILM PA is Dr. Bhavin Rawal, an AHFMR

ForeFront Intern. The ForeFront Internship Program provides opportunities for university graduates to learn the business aspects of the health industry through a combination of training courses and on-the-job experience. The program addresses the need for managers with commercialization expertise in Alberta-based health and medical-products companies.

Dr. Rawal is now leading the commercialization of bioFILM PA. The product has already received Health Canada approval, and Innovotech is conducting the quality-testing that

will certify the test kit for use in hospitals.

"There's a lot left to do in biofilms: we have plans for test kits for both staphylococcus and fungal biofilm infections," notes Boutilier. "In the next few years, we hope to bring an agricultural product to market to address a biofilm problem in agriculture that is of the same magnitude as the biofilm problem in human health. We may be a small company, but we've got big plans."*



Food and mood

Brenda Leung studies the link between nutrition and depression in pregnant women and new mothers.



BRENDA LEUNG is a Doctor of Naturopathic Medicine (N.D.) by

training. Her interest in pure research grew while she was practising as a naturopathic doctor in Surrey, B.C. Intrigued by questions arising in her clinical practice—questions for which she had no answers—she decided on a period of further study. She chose the area of nutrition in maternal mental health as one where she could put her naturopathic experience to good use.

At the University of Calgary Leung first tackled master's studies, in the Department of Community Health Sciences. Her supervisor was Dr. Marja Verhoef, a Canada Research Chair in Complementary Medicine and one of the few scientists in Canada doing research in this field. In 2005 Leung began doctoral work under research psychologist Dr. Bonnie Kaplan in the Department of Pediatrics. Leung's Ph.D. studies are funded by AHFMR and the Alberta Mental Health Board through a new and innovative partnership.

Combining her interests in nutritional epidemiology



and mental health, Leung has designed a study to examine the link between nutrition and depression in pregnant women and new mothers. She notes that her work in the mental-health area is filling a gap. "Most nutrition-based studies deal with physical-health issues, such as diabetes and heart disease," she says. Two aspects of Leung's work break

new ground: her long-term approach to this study of nutrition in depression; and her focus on pregnant women, who are often excluded in such studies.

Leung began work on the first stage of this project in September 2006 and plans to have preliminary data by late 2009. Working with a seven-member team, including the directors of three prenatal clinics in Cal-

Is there a connection between certain nutrients and mood?

gary, Leung is recruiting women who are in the first trimester of pregnancy to help her find out whether there is any link between diet and depression. Leung's study will follow these women throughout their pregnancies and after their children are born. She hopes that it will determine what pregnant women are really eating, and whether there is any connection between certain nutrients (or combinations of nutrients) and mood.

Depression is one of the fastest-rising medical conditions in the world. The World Health Organization (WHO) ranks depression second on the list of disabilities that reduce productivity worldwide. Leung also points

out that depression in women can have far-reaching effects. "Depressed mothers may be less capable of caring for their children, which may result in poorer child development, mentally and physically." ❖

About the researcher

Brenda Leung is a Ph.D. student at the University of Calgary. Her research is supported by AHFMR, in partnership with the Alberta Mental Health Board.

Recommended reading

Ryrie I, Cornah D, Van de Weyer C. Food, Mood, and Mental Health. *Mental Health Today*, 2006 Feb;6(1):23-26.

Recommended website

Mental Health Foundation (UK)
<http://www.mentalhealth.org.uk>

AHFMR funding partners

The Alberta Heritage Foundation for Medical Research (AHFMR) has contributed more than \$900 million to Alberta's health-research community. The Foundation also relies on the contributions of many partners in building and sustaining health research in this province. To mention just a few, these partners include

- the Government of Alberta and its related ministries and programs;
- federal granting agencies such as the Canadian Institutes of Health Research, the Canada Foundation for Innovation, and the Canadian Health Services Research Foundation;
- international funding partners like the Wellcome Trust and the National Institutes of Health; and
- non-profit and voluntary funding agencies such as NeuroScience Canada, the Heart and Stroke Foundation, the Canadian Diabetes Association, and the National Cancer Institute of Canada.

What is a naturopathic doctor?

An N.D. is a primary-care medical practitioner who has earned the degree of Doctor of Naturopathic Medicine (N.D.). Naturopathic doctors capitalize on nature's self-healing process to restore and maintain optimum health in their patients. Naturopathic practice does not include invasive medical treatments such as surgery, injections, X-rays, or prescription drugs.

Prerequisites for study toward an N.D. degree include three years of pre-medical sciences at university with a grade point average of 3.0 or higher. The candidate must then complete a four-year full-time program in basic science, clinical and naturopathic disciplines, and clinical experience at an accredited school of naturopathic medicine. More than 4,500 hours of classroom time and 1,500 hours of supervised training go into the making of a naturopathic doctor.

Naturopaths, naturopathic physicians, naturopathic consultants, and naturopathic practitioners are sometimes incorrectly referred to as naturopathic doctors. The difference is in the level of education and training. A naturopathic doctor in Canada must have an N.D. degree from an educational facility accredited by the Canadian Association of Naturopathic Doctors (CAND).

For more information, visit the Canadian Association of Naturopathic Doctors (CAND) website at <http://www.cand.ca>

Following up

Consulting the public on controversial issues

■ THE VALUE OF PUBLIC CONSULTATIONS ON CONTROVERSIAL NEW TECHNOLOGIES is generally accepted, but it is difficult to consult with people on topics that few of us know anything about. This was the challenge facing University of Calgary professor Dr. Edna Einsiedel in 2000 when she developed a pilot consultation process on xenotransplantation.

Xenotransplantation is the transfer of living cells, tissues, or organs from one species to another—for example, the transplanting of a pig kidney into a human. The promise of xenotransplantation is a potentially unlimited supply of needed tissues, which could make transplant waiting lists a thing of the past. However, many people have serious medical concerns about the risk of transmitting viruses from animals to humans, as well as about the ethics of “engineering” animals solely to meet human needs.

The process that Dr. Einsiedel tailored for the xenotransplantation issue is called a *citizen jury*, a “deliberative” model of consultation in which



Dr. Edna Einsiedel

individuals learn about an issue and discuss it before giving their opinions. In pilot projects in Calgary and Edmonton, citizens were recruited to juries. They received reading materials before attending a week-end-long forum. At the forum scientific, legal, and ethics experts representing a variety of viewpoints gave presentations and answered questions. Jurors then discussed the issue and reached a conclusion.

Thus flight-tested, the citizen-jury process went on to six other cities in 2001, serving as part of a nationwide public consultation initiated by Health

Canada to help decide whether Canada should proceed with xenotransplantation. Dr. Einsiedel was a member of the public advisory group of the Canadian Public Health Association which led that consultation.

In their final report the group recommended that Canada should not proceed with xenotransplantation at that time. They reached the conclusion that not enough was known about the health risks of such transplants; that alternatives needed to be explored; and that the existing regulations and legislation governing xenotransplantation in Canada were inadequate. ✽

About the researcher

Dr. Edna Einsiedel is a professor in the Faculty of Communication and Culture at the University of Calgary. The pilot consultation projects were supported by the *Health Research Fund*, administered by AHFMR on behalf of Alberta Health and Wellness.

Recommended website
Public Consultation
on Xenotransplantation
<http://www.xeno.cpha.ca>

